REMARKS

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks. Support for the claim amendments are found throughout the specification, including in cancelled claims 2-5, as well as page 13, line 20 to page 14, line 1.

Claim of Priority under 35 U.S.C. §119

Applicants thank the Examiner for acknowledgement of the claim for priority under 35 U.S.C. §119 and receipt of the priority document.

The Rejection of Claims 1-6 under 35 U.S.C. §112, 1st Paragraph

The Examiner asserts that claims 1-6 contain subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. More specifically, the Examiner asserts that the specification fails to provide a written description of any method for producing any target substance using any bacterium belonging to the genus *Escherichia* wherein said bacterium contains an RMF protein of any amino acid sequence and biological source that does not function normally due to any genetic modification.

Applicants respectfully submit that the claims as amended are now fully and adequately described in the specification. The claims have been amended to limit the genus *Escherichia* to the species *Escherichia coli*, and the limitation regarding the RMF protein now specifies that the inactivity of the RMF protein, caused by a rmf gene mutation, results in greater production of an L-amino acid by the bacterium. Applicants point to the specification at page 28, and specifically to Table 2, which describes the

increase in L-lysine accumulation as a result of the rmf gene mutation.

Furthermore, applicants assert that the present specification provides sufficient written description of any L-amino acid as a target substance for the following reasons. Applicants were the first to disclose that the production of L-lysine can be improved by disrupting the rmf gene. While the rmf gene is expressed during the stationary phase of the culture and the protein translation activity is decreased in the wild-type strain, Applicants surprisingly found that the decrease of protein translation activity is prevented or reduced in a strain in which the normal RMF protein does not function normally (see page 17, lines 15-22). Therefore, clearly the present specification describes that productivity of an L-amino acid other than L-lysine is also improved in a strain in which the RMF protein does not function normally.

Moreover, it is well-known in the art that inactivation of a protein via mutating the gene encoding said protein or the sequences that control the gene, when these sequences are known, will lead to inactivation of the protein activity. Therefore, in view of the knowledge in the art, a modification other than that used in the Examples of the present specification can be used and still remain within the scope of the present invention.

Therefore, applicants respectfully submit that the claims as amended are adequately described by the specification and request that the rejection be withdrawn.

Claims 1-6 are also rejected under 35 U.S.C. §112, 1st paragraph for non-enablement. The Examiner asserts that the SEQ ID Nos. of the inactivated rmf gene are critical or essential to the practice of the invention, but not included in the claims. Applicants respectfully disagree and set forth the following arguments. The strain having

L-lysine producing activity has been deposited under the provisions of the Budapest Treaty and assigned accession number FERM BP-5252. Since this deposit is properly identified in the specification, and the evidence of deposit was filed with the application on the filing date of December 21, 2001, the specification adequately provides a starting material so that a person of ordinary skill in the art may practice the claimed method without undue experimentation.

Using this provided starting material, or any other known L-amino acid producing stain, a strain having a disrupted rmf gene may be obtained according to the methods of the present invention. At the time the present specification was filed, the rmf gene from *E. coli* was known (as evidenced by Chou et al. and GenBank accession number D90733, printout attached). Based on the known sequence combined with the description in Example 2 of the specification, one skilled in the art would be enabled to obtain the inactivated rmf gene and RFM protein of the present invention.

Furthermore, an inactivated rmf gene having a different sequence other than that described in the present invention is within the scope of the present invention, so long as the rmf gene is inactivated. Since the method for disrupting a known gene is well-known to those having ordinary skill in the art, obtaining a disrupted, and therefore inactivated rmf gene having any sequence, is well within the skill of the ordinarily skilled artisan.

In light of the foregoing arguments, one of ordinary skill in the art would be enabled to practice the steps of the claimed method, and therefore, applicants respectfully submit that the claims are fully enabled and request that the rejection be withdrawn.

Paragraph 5 of the Examiner's office action also rejects claims 1-6 under 35 U.S.C. §112, first paragraph, asserting that the claims contain subject matter which was

not described in the specification in an enabling fashion. The Examiner acknowledges that molecular biological and genetic manipulation techniques are well known and the skill of the artisan is well developed, however still asserts that, particularly under the factors set forth in *In re Wands* (citation omitted), experimentation to practice the invention is undue.

Applicants respectfully disagree, and in light of the foregoing amendments, respectfully submit that the invention as claimed is adequately enabled by the specification. The Examiner seems particularly worried about the lack of a source designation for the mutated rmf gene, or the absence of any sequence information for the rmf gene. Applicants submit that the claims as amended recite that the rmf gene mutation results in an inactive RMF protein, and that the result of this mutation and inactivation is greater production of a target substance as compared to if the RMF protein were active. Such determinations are clearly within the skill of the artisan, as these experiments are fully described in the Examples in the specification. The source of the mutated rmf gene is adequately enabled since an L-lysine producing strain has been deposited under the provisions of the Budapest Treaty, the rmf gene sequence is known, and the methods for obtaining a disrupted gene are also known in the art. Therefore, for these reasons and others stated above, Applicants respectfully submit that one of skill in the art, armed with Applicants' specification and the deposit information contained therein, would be enabled to practice the invention as claimed, and further sequence information is not required. Therefore, Applicants respectfully submit that the claims are fully enabled and described in the specification and Applicants request that the rejection be withdrawn.

The Rejection of Claims 1-6 under 35 U.S.C. §112, 2nd Paragraph

The Examiner has rejected claims 1-6 under 35 U.S.C. §112, 2nd paragraph, asserting that the phrase "wherein an RMF protein of the bacterium belonging to the genus Escherichia does not function normally" is vague and indefinite. Applicants have amended the claims to remove this language. Applicants respectfully submit that the claims as amended are definite and request that the rejection be withdrawn.

The Rejection of Claims 1-6 under 35 U.S.C. §102(b)

The Examiner has rejected claims 1-6 as being anticipated by Chou et al. under 35 U.S.C. §102(b). Applicants respectfully submit that the claims as amended are not anticipated by the Chou reference for the following reasons. Firstly, Applicants have added the limitation to the claims that the rmf gene mutation, and subsequent RMF protein inactivation, results in production of an L-amino acid in quantities larger that if the RMF protein were active in the bacterium.

Chou specifically states that protein activity, and hence quantity, cannot be predicted by inactivation of the RMF protein, but that such an outcome is dependent upon the expression system used. If fact, the reference shows that when a lac promoter system was used, there was no increase in protein activity (see Fig. 3 of Chou). Furthermore, Chou only demonstrates an increase in expression of β-galactosidase upon inactivation of rmf gene when a ph-induced expression system is employed (see Fig. 2 of Chou). The claims, as amended, are limited to production of L-amino acids, not β-galactosidase. There is no mention in Chou of L-amino acid production. Therefore, Chou fails to show a reproducible method practicable by one of skill in the art for producing an L-amino acid

in increased quantities by inactivating the RMF protein via mutation of the rmf gene, and actually teaches away by demonstrating the expression system dependency of the rmf mutation.

For at least the foregoing reasons, Applicants respectfully submit that the Chou fails to identically disclose or describe the subject matter recited in amended claims 1 and 6. Accordingly, Applicant respectfully requests withdrawal of the rejections thereof.

Conclusion

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Fronda believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, he is invited to call on the number below.

It is not believed that extensions of time are required beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the undersigned respectfully requests that she be contacted immediately.

Att'y Dkt. No. US-146O U.S. App. No: 10/023,711

Respectfully submitted,

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Date: December 23, 2003